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Outlook

WINTER 2017-18



Washington
University in St. Louis
SCHOOL OF MEDICINE

Confronting
disparities



Esme “Ezzy” Hodge, left, of Bristol, U.K., recently took her first independent steps following selective dorsal rhizotomy (SDR) surgery at St. Louis Children’s Hospital. Neurosurgeon T.S. Park, MD, has performed SDR on more than 3,700 patients with cerebral palsy worldwide. In most cases, the procedure permanently removes spasticity, enabling patients to walk again. See page 24.



TIM PARKER PHOTOS

COVER Will Ross, MD, MPH, nephrologist and associate dean for diversity, grew up “the poorest of the poor.” His earliest memories are ones of violence. Today, he is a national leader speaking out against health disparities and has ingrained core principles of understanding and treating the underserved into the medical school curriculum. See page 18.

FEATURES

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Engineered stem cells could revolutionize arthritis therapy and joint replacement.

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The transformative influence of a doctor who hasn’t forgotten his past.

24 ‘Future we only dreamed of’

T.S. Park, MD, is one of the few neurosurgeons worldwide performing a procedure that restores mobility in children with cerebral palsy.



Outlook

Washington University School of Medicine

OUTLOOK.WUSTL.EDU WINTER 2017-18



Envisioning cells like little machines, Farshid Guilak, PhD, is reprogramming them to fight arthritis. In the lab, his team successfully has grown a living human hip ball joint that suppresses inflammation. See page 12.

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A dedication ceremony recently was held for the Debra and George W. Couch III Biomedical Research Building. The couple's \$10 million gift supports one of the medical school's highest priorities: personalized medicine. See page 30.

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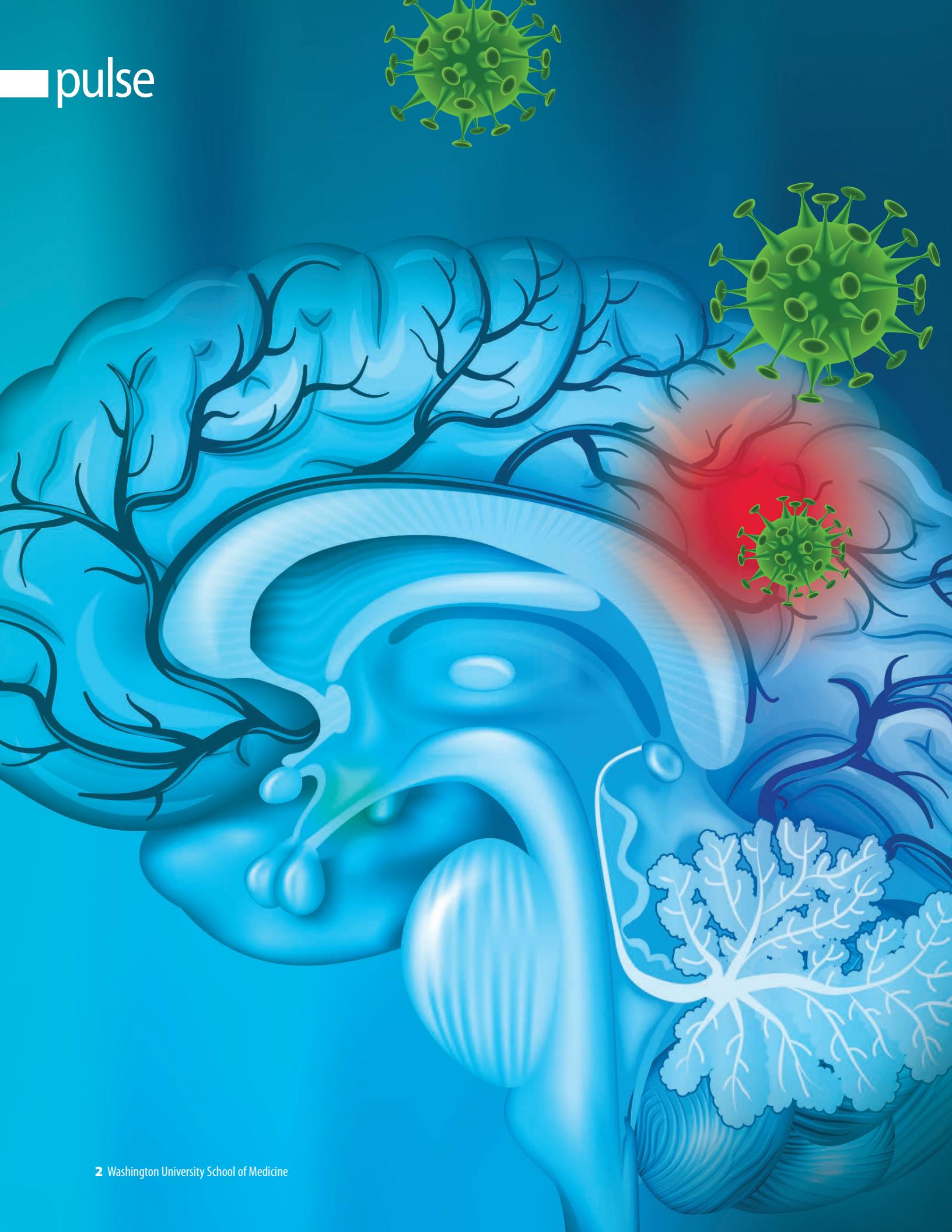
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Cancer weapon

Zika virus kills glioblastoma stem cells in early research

BY TAMARA BHANDARI

While Zika virus causes devastating damage to the brains of developing fetuses, it one day may be an effective treatment for glioblastoma, a deadly form of brain cancer. New research from Washington University School of Medicine and the University of California San Diego School of Medicine shows that the virus kills brain cancer stem cells, the kind of cells that are most resistant to standard treatments.

“We showed that Zika virus can kill the kind of glioblastoma cells that tend to be resistant to current treatments and lead to death,” said Michael S. Diamond, MD, PhD, the Herbert S. Gasser Professor of Medicine at Washington University and the study’s co-senior author.

The findings are published Sept. 5 in *The Journal of Experimental Medicine*.

The standard glioblastoma treatment is aggressive — surgery, chemotherapy and radiation — yet most tumors recur within six months. A small population of glioblastoma stem cells often survives the onslaught and continues to divide, producing new tumor cells to replace the ones killed by the cancer drugs.

In their neurological origins and near-limitless ability to create cells, glioblastoma stem cells reminded

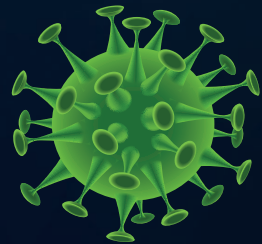
postdoctoral researcher Zhe Zhu, PhD, of neuroprogenitor cells, which generate cells for the growing brain. Zika virus specifically targets and kills neuroprogenitor cells.

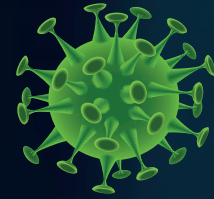
Collaborating with co-senior authors Diamond and Milan G. Chheda, MD, of Washington University, and Jeremy N. Rich, MD, of UC San Diego, Zhu tested whether the virus could kill stem cells in glioblastomas removed from patients at diagnosis. They infected tumors with one of two strains of Zika virus. Both strains spread through the tumors, killing the cancer stem cells while largely avoiding other tumor cells.

The findings suggest that Zika infection and chemotherapy-radiation treatment have complementary effects. The standard treatment kills the bulk of the tumor cells but often leaves the stem cells intact to regenerate the tumor. Zika virus attacks the stem cells but bypasses the greater part of the tumor.

To find out whether the virus could help treat cancer in a living animal, the researchers injected either Zika virus or salt water (a placebo) directly into the brain tumors. Tumors were significantly smaller in the Zika-treated mice two weeks after injection, and those mice survived significantly longer.

The idea of someday injecting a virus notorious for causing brain damage into people’s brains seems alarming, but Zika may be safer for use in adults because its primary targets — neuroprogenitor cells — are rare in the adult brain. The fetal brain, on the other hand, is loaded with such cells, which is part of the reason why Zika infection before birth produces widespread and severe brain damage.





Diamond



Chheda

Q&A

with Mike Diamond and Milan Chheda

How did you come up with the idea of using Zika to treat glioblastoma?

Diamond: It was really the idea of Zhe Zhu, who was a postdoc with Jeremy Rich. He emailed me several times and said he wanted to do it. I said, “That’s crazy, I don’t want to do that.” Because I knew that a related virus — West Nile — had been tried 50 years ago and it made things worse. It caused serious brain infections and did not cure the cancer. So I said, “That’s not going to work. That’s not safe.” But he kept on asking until I agreed to let him try. Jeremy sent him over to my lab for what was supposed to be three months and turned into a year. And at some point we gathered enough data to look at which cells were being infected and found that it was not replicating throughout the brain and then I no longer had reservations. After we had established that the virus could specifically infect the stem cells, we needed someone with neuro-oncologic expertise. Milan took on a major role at that point.

What has been the response to the study?

Chheda: We’ve received emails from patients all over the world. They say that their loved ones or a friend or they themselves are in this dire situation and ask if they can try Zika.

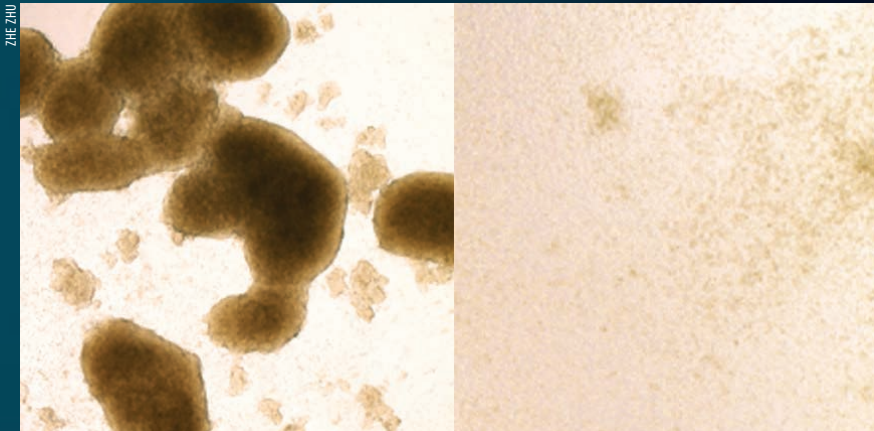
We tell them that it’s not FDA-approved, it hasn’t been proven safe or effective, but some people say they understand that and they want to try it anyway. We’ve been asked if we can bring the virus to some other place, like Mexico, where FDA rules don’t apply so they can try it. And of course we can’t do that, but it just goes to show how desperate people are for any bit of hope.

What do you say to the people who contact you?

Chheda: I ask if they want to speak on the phone. They tell me about their current treatment or plans for treatment. The one thing that stands out is that throughout the world, almost everyone is treated the same way when they are first diagnosed. And universally the situation is dire no matter where you live. I tell them that we’re working on getting to human trials, but we’re talking about at least a year and a half before anything could potentially be tested in humans.

What do you have to do before you can test it in people?

Diamond: We are trying to get some guidance on that from the FDA. Because of the dire nature of the disease, the bar might not be as high as we thought. The key issue, of course, is safety. Although discussions are planned, the FDA likely will require that giving Zika doesn’t make things worse in mice, and that we can manufacture the virus according to good manufacturing practices. But they may want more, too; it’s not totally clear yet.



From left, brain cancer stem cells before and after Zika treatment. A new study shows that the virus, known for killing cells in the brains of developing fetuses, could be redirected to destroy the kind of brain cancer cells that are most likely to be resistant to treatment.

Immune therapy targets certain blood cancers

Siteman Cancer Center is one of the first U.S. centers to offer an immune therapy targeting advanced non-Hodgkin lymphoma (NHL) in adults. Yescarta, a chimeric antigen receptor (CAR)-T cell therapy, is the second gene therapy approved by the Food and Drug Administration (FDA). Washington University doctors and researchers were involved in clinical trials leading to its approval.

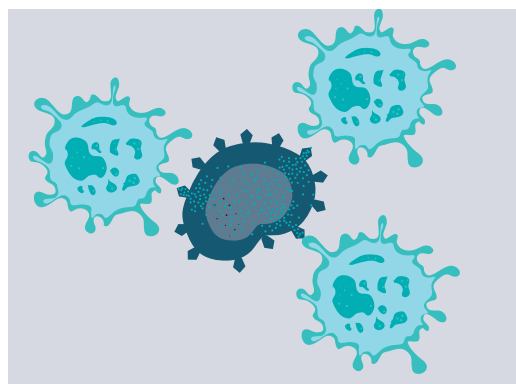
In cancer patients, the immune system's T cells lose the ability to recognize and attack cancer cells. CAR-T cell therapy involves isolating a patient's T cells from the blood and genetically altering — or supercharging — those cells to home in on cancer cells.

Once a CAR-T cell finds its target, it behaves as any T cell should — triggering a chain reaction that destroys the cancerous cell. There is evidence that some CAR-T cells may maintain active surveillance and ramp up again in response to cancer recurrence. CAR-T cells can be programmed to lock on to different cell surface features, suggesting the strategy could expand to other cancers.

The therapy for NHL is available only to adult patients whose cancer has not responded to standard treatments, including chemotherapy and bone marrow transplantation. Kite Pharma developed the new treatment.

Because the therapy induces a heightened immune response, there can be a range of side effects, from fever and shortness of breath to kidney failure and seizures. Many of the side effects are manageable, but some are severe and a few can be life-threatening, which is why the first centers selected to administer the new therapy are those with extensive expertise in treating blood cancers.

The first cancers to be treated with CAR-T cell therapy include certain types of large B-cell lymphomas in adults and acute lymphoblastic leukemia (ALL) in children. Clinical trials of CAR-T therapy have shown what doctors have called remarkable remission rates among children with ALL and adults with lymphomas and multiple



SARA MOSER

T cells are isolated from the blood and modified to home in on the type of cell affected by the cancer.

myeloma. In patients whose disease has not responded to standard therapies or has relapsed, CAR-T therapy has achieved from 40 to 80 percent remission rates. Some patients have remained in remission for several years.

Doctors at Siteman also are evaluating or soon will be evaluating CAR-T therapy via clinical trials for sarcoma, melanoma, lung and ovarian cancer, leukemia and multiple myeloma.

Potential new therapy relieves chronic itch

New research has identified immune signaling molecules that may underlie chronic itching, an unrelenting urge to scratch.

The researchers also discovered that patients with chronic idiopathic pruritus, a type of itch from an unknown cause, improve when given the rheumatoid arthritis drug tofacitinib (Xeljanz). Earlier attempts to treat their itching with other

anti-inflammatory drugs had been unsuccessful. Within one month of taking tofacitinib, all five study patients experienced marked relief: They stopped scratching, started sleeping again and returned to more productive lives.

"Obviously, we'll need to do a larger study, but the early results are very encouraging," said Brian S. Kim, MD, an assistant professor of medicine and co-director of the Center for the Study of Itch.

As part of the study, the researchers showed that the immune signaling molecule interleukin-4 (IL-4) activates sensory neurons in mice and people. IL-4 signaling can jumpstart chronic itching in the setting of inflammation but also independently of pathways directly linked to inflammation, they found. Chronic idiopathic pruritus, for example, isn't associated with inflammation.

Kim's team, led by MD/PhD student and first author Landon K. Oetjen, engineered mice to have sensory neurons that lacked the ability to respond to IL-4. When exposed to stimuli that should have made them itch, the mice didn't scratch.

The researchers then determined that IL-4 stimulates JAK1, a key protein within nerve cells that may be a uniquely sensitive target for multiple types of itch. The drug tofacitinib blocks this protein.



GETTY IMAGES

Skin cells turned into human motor neurons

Scientists working to develop treatments for neurodegenerative diseases have been stymied by the inability to grow human motor neurons in the lab. Motor neurons drive muscle contractions, and their damage underlies devastating diseases such as amyotrophic lateral sclerosis and spinal muscular atrophy.

Now, School of Medicine scientists have converted skin cells from healthy adults directly into motor neurons without going through a stem cell state.

The technique makes it possible to study motor neurons of the human central nervous system in the lab. Unlike commonly studied mouse motor neurons, human motor neurons growing in the lab would be a new tool since researchers can't take neuron samples from living people but can easily take skin samples.

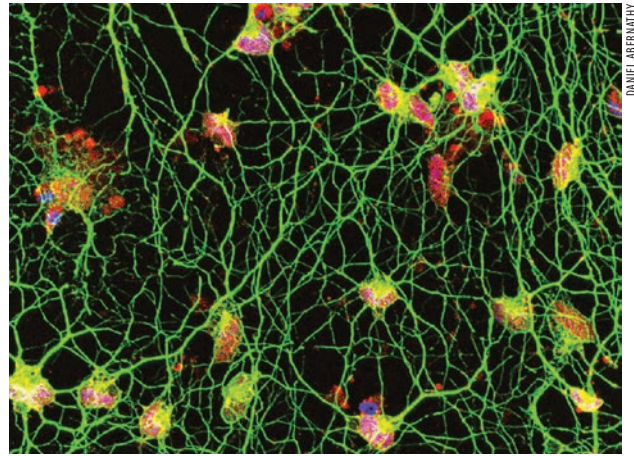
Avoiding a stem cell state allows the resulting motor neurons to retain the age of the original skin cells and, therefore, the age of the patient. Maintaining the chronological age of these cells is vital when studying neurodegenerative diseases that develop in people at different ages and worsen over decades.

"In this study, we only used skin cells from healthy adults ranging in age from early 20s to late 60s," said senior author Andrew S. Yoo, PhD, an assistant professor of developmental biology.

To convert skin cells into motor neurons, the researchers exposed the skin cells to molecular signals that are usually present at high levels in the brain. Past work by Yoo and his colleagues — then at Stanford University — showed that exposure to two short snippets of RNA, called miR-9 and miR-124, turned human skin cells into neurons.

After much experimentation, researchers found that adding two more signals to the mix — transcription factors called ISL1 and LHX3 — turned the skin cells into spinal cord motor neurons in about 30 days.

The combination of signals tells the cell to fold up the genetic instructions for making



DANIEL ABERNATHY

Scientists have discovered a new way to convert human skin cells directly into motor neurons (above).

skin and unfurl the instructions for making motor neurons.

The researchers said the converted motor neurons compared favorably to normal mouse motor neurons. Future work studying neuron samples donated from patients after death is required to determine how precisely these cells mimic native human motor neurons.

Medical students not trained to prescribe marijuana

Although 29 states and the District of Columbia allow marijuana use for medical purposes, few medical students are being trained how to prescribe the drug, according to School of Medicine research.

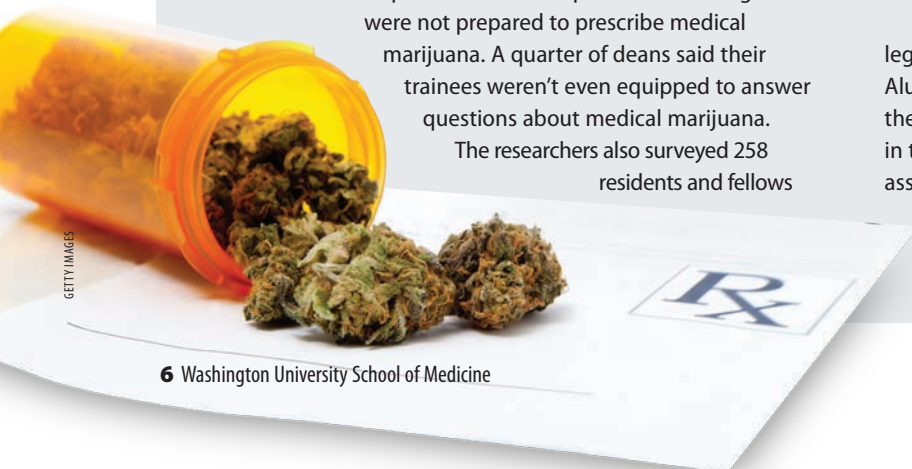
The research team, led by first author Anastasia B. Evanoff, a third-year medical student, sent surveys to curriculum deans at 172 medical schools in North America, including 31 that specialize in osteopathic medicine, and received 101 replies. Two-thirds reported that their graduates were not prepared to prescribe medical marijuana. A quarter of deans said their trainees weren't even equipped to answer questions about medical marijuana.

The researchers also surveyed 258 residents and fellows

who earned their medical degrees from schools around the country. Nearly 90 percent felt they weren't prepared to prescribe medical marijuana, and 85 percent said they had not received any education about the drug during medical school or residency.

In examining a curriculum database maintained by the Association of American Medical Colleges, the researchers found that only 9 percent of medical schools had reported teaching their students about medical marijuana.

"Medical education needs to catch up to marijuana legislation," said senior author Laura Jean Bierut, MD, the Alumni Endowed Professor of Psychiatry and a member of the National Advisory Council on Drug Abuse. "Physicians in training need to know the benefits and drawbacks associated with medical marijuana so they know when or if, and to whom, to prescribe the drug."



GETTY IMAGES

Algorithm could speed Parkinson's diagnosis

Before symptoms become pronounced, there is no reliable way to identify who is on track to develop Parkinson's disease, a debilitating movement disorder.

But School of Medicine researchers have analyzed Medicare claims data of more than 200,000 people to develop an algorithm to predict whether a patient one day will be diagnosed with Parkinson's. The algorithm relies on information in patients' medical records, such as tests and diagnoses of various medical conditions.

"Using this algorithm, electronic medical records could be scanned and physicians could be alerted to the potential that their patients may need to be evaluated for Parkinson's

disease," said Brad A. Racette, MD, the Robert Allan Finke Professor of Neurology and the study's senior author.

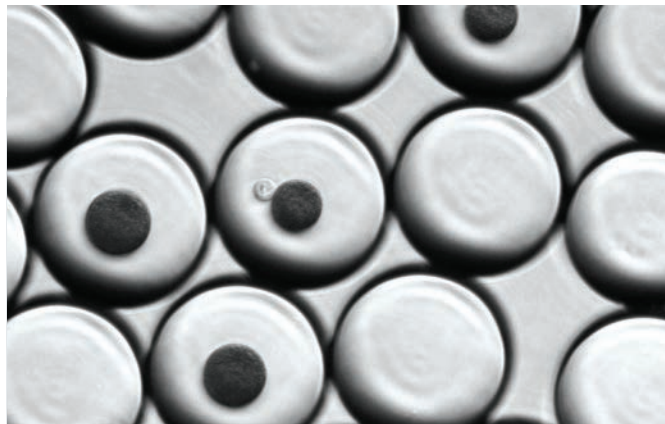
"One of the most interesting findings is that people who are going to develop Parkinson's have medical histories that are notably different from those who

don't develop the disease. This suggests there are lifelong differences that may permit identification of those likely to develop the disease decades before onset."

The study is available online in the journal *Neurology*.

Many of the claims codes referred to problems already known to be associated with Parkinson's such as tremors, posture abnormalities, psychiatric or cognitive dysfunction, gastrointestinal problems, sleep disturbances, fatigue and trauma, including falls. Other factors associated with the disease included weight loss and multiple forms of chronic kidney disease.

In the 18 months before diagnosis, people endured a flurry of doctor visits and medical tests. Most likely, their symptoms were worsening, and their doctors were running test after test, looking for the cause, said Racette. Using this algorithm potentially could help reduce unnecessary tests and speed the process of diagnosis, he said.



In single-cell RNA sequencing, individual cells are suspended in water droplets that contain a coated bead. When the cell is purposefully broken apart, the coated bead captures the cell's RNA so it can be analyzed. Above, the large circles are water droplets. Smaller, dark circles are the coated beads. In the center, a single translucent kidney cell from a mouse touches one of the beads. Each droplet is about the diameter of a human hair.

Facebook CEO supports Human Cell Atlas projects

The Chan Zuckerberg Initiative has awarded pilot grants to two School of Medicine researchers, supporting projects contributing to the Human Cell Atlas. This is an international effort to create a detailed map of all cells in the human body. Charting the locations of individual cells, unraveling their genetics and revealing how they interact to regulate health can shed light on how things go wrong and result in disease.

Facebook co-founder Mark Zuckerberg and his wife, Priscilla Chan, MD, established the Chan Zuckerberg Initiative with the goal of eliminating disease.

Samantha A. Morris, PhD, an assistant professor of developmental biology and of genetics, and Benjamin D. Humphreys, MD, PhD, the Joseph Friedman Associate Professor of Renal Diseases in Medicine, each have received one year of support to conduct single-cell RNA sequencing with a focus on cells in the kidney, liver and small intestine. Their labs will map out the relationships between and plumb the biological depths of every one of the millions of individual cells that make up each of those organs.

Humphreys, a kidney specialist, is investigating why some patients with diabetes experience kidney failure quickly while others gradually develop kidney damage.

Morris is focused on cells in the liver and small intestine. A goal of her research is to engineer a working intestine as a therapy for short bowel syndrome. The condition can lead to malnutrition after a portion of the bowel has been removed, often to treat conditions such as cancer or Crohn's disease.

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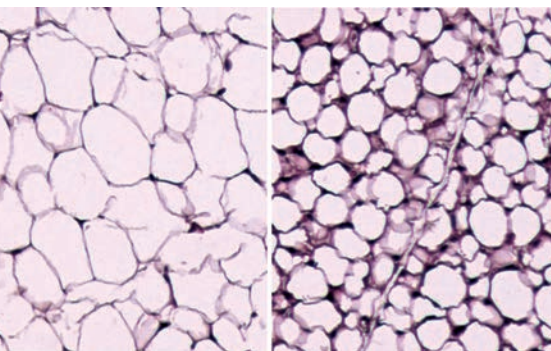


Scientists convert bad body fat in mice into good fat

Good fat in our bodies helps burn calories, while the bad fat hoards calories, contributing to weight gain and obesity. New research has identified a way to convert bad, white fat into good, brown fat, at least in mice.

White fat stores calories and pads our bellies, hips and thighs. Brown fat, found near our necks and shoulders, burns calories through a process that generates heat.

Beige fat — an intermediary between white and brown fat — was discovered in adult humans in 2015. It functions



White fat cells from a normal mouse, left, and from a mouse lacking the PexRAP protein.

more like brown fat and can protect against obesity, said first author Irfan J. Lodhi, PhD, an assistant professor of medicine in the Division of Endocrinology, Metabolism and Lipid Research.

His team created a genetic strain of mice that didn't

make a specific protein called PexRap in white fat cells. The researchers found that blocking the protein triggered the white fat to begin to brown into beige fat, causing the fat cells to burn calories. The mice with more beige fat were leaner than their littermates, even when they ate the same amount of food. They also burned more calories.

Lodhi said if PexRAP could be blocked safely in human white fat cells, people might have an easier time losing weight.

Hultgren elected to National Academy of Medicine



Scott J. Hultgren, PhD, the Helen L. Stoever Professor of Molecular Microbiology, has been elected to the National Academy of Medicine, a part of the National Academy of Sciences. Membership is one of the highest honors in the field of medicine.

Hultgren has made groundbreaking contributions to understanding urinary tract infections.

Can laughing gas help prevent suicide?

Researchers are studying the use of nitrous oxide — laughing gas — as a treatment for patients who are hospitalized due to suicidal thoughts.

Most standard antidepressant drugs affect norepinephrine and serotonin receptors in the brain, but can take weeks to improve a person's symptoms. Nitrous oxide interacts with a different type of receptor in the brain — NMDA glutamate receptors — sometimes improving symptoms within hours.

"Nitrous oxide may very quickly improve depression in these patients," said Peter Nagele, MD, an associate professor of anesthesiology and of genetics. "The gas has very few side effects because it leaves the body very quickly once people stop breathing it. However, it appears from our previous research that the antidepressant effects of nitrous oxide may linger in the brain long after the drug is out of the body."

In this new study — funded by a grant from the American Foundation for Suicide Prevention — people who have attempted suicide will breathe a mixture of oxygen and nitrous oxide for one hour, every other day, for one week.

Half of the anticipated 50 study patients will receive this mixture; the other half will receive oxygen — but without the nitrous oxide — over the same amount of time. All participants will receive antidepressant drugs or talk therapy normally prescribed during such a hospitalization.

Ongoing follow-up visits will monitor the participants' mental state. "If such problems re-emerge, the study is designed to provide 'booster' treatments with nitrous oxide, which we believe will continue to lower the likelihood of future suicidal thoughts," said Charles R. Conway, MD, a professor of psychiatry.





Too many brain connections may be at root of autism

Rodents that lack a gene linked to autism form too many connections between neurons and have difficulty learning, according to a School of Medicine study. The findings suggest that some autism symptoms may stem from miscommunication among brain cells.

"This study raises the possibility that there may be too many synapses in the brains of patients with autism," said senior author Azad Bonni, MD, PhD, the Edison Professor of Neuroscience and head of the Department of Neuroscience. "You might think that having more synapses would make the brain work better, but that doesn't seem to be the case."

Autism, a neurodevelopmental disorder, is characterized by social and communication challenges.

Of the many genes linked to autism, six are known as ubiquitin ligases because they attach a molecular tag, called ubiquitin, to

proteins. These tags function like a work order, telling the rest of the cell how to deal with the tagged proteins: This one should be discarded, that one should be rerouted to another part of the cell.

Some people with autism carry a mutation that prevents one of their ubiquitin genes from working properly. But it is poorly understood how problems with tagging proteins affect the brain's hardwiring and operation, and why such problems may lead to autism.

To understand the role of ubiquitin genes in brain development, Bonni, first author Pamela Valnegri, PhD, and colleagues removed the ubiquitin gene RNF8 from neurons in the cerebellums of young mice.

Neurons without RNF8 formed about 50 percent more functioning synapses — the connections that allow neurons to send signals to each other — than those with the gene.

Mutations in a gene linked to autism cause neurons to form too many connections in rodents. The findings suggest that malfunctions in communication between brain cells could be at the root of autism.

The cerebellum is indispensable for movement and learning new motor skills. Some common symptoms of autism — such as motor incoordination and a tendency to walk tippy-toed — involve control of movement.

The animals missing the RNF8 gene walked normally and appeared coordinated, but were unable to learn new motor skills.

The researchers since have tested other autism-associated ubiquitin genes. All of them led to an increase in synapses when inhibited, suggesting that too many synapses could be the reason why these genes are linked to autism. If this hypothesis proves true in people, finding ways to control the number of synapses might benefit those with autism.

Medical school physicians, staff aid hurricane victims

Washington University faculty and staff helped with emergency relief efforts after devastating hurricanes hit the southern U.S. and the Caribbean this summer. While they were away, their colleagues pulled together to keep operations on the Medical Campus running as normal.



Stephen Liang, MD, center foreground, and teammates in Missouri Task Force 1.

STEPHEN LIANG, MD

Assistant professor of medicine and of emergency medicine

Liang responded to Hurricane Harvey as a member of Missouri Task Force 1, part of the Federal Emergency Management Agency's (FEMA) National Urban Search & Rescue Response System. As Harvey made landfall in Houston, FEMA called on Missouri Task Force 1 to deploy a team specialized in swift-water rescue. The task force rescued or evacuated about 400 people, as well as many pets. Liang was principally responsible for keeping the team healthy as it conducted strenuous operations. He also conducted medical checks on people brought to safety by his teammates.

DOUGLAS CHAR, MD

Professor of emergency medicine

A team member with the National Disaster Medical System (NDMS), Char serves as the medical director of a Missouri group of more than 100 doctors, nurses, paramedics and other health-care professionals. During Hurricane Harvey, Char's group was assigned to Dallas. Later, he traveled to Austin as chief medical officer and consultant for a U.S. Department of Health and Human Services (HHS)



Douglas Char, MD, in the crisis room.

team handling hurricane-related flooding in Texas and Louisiana. He helped decide which shelters needed medical services and for how long, and compiled reports on disease outbreaks. After two weeks, he flew to Washington, serving as the overnight chief medical officer — dealing with Hurricanes Harvey, Irma and Maria — in the HHS crisis room, which is staffed 24 hours a day in national emergencies.



COURTESY OF BOONE COUNTY FIRE PROTECTION DISTRICT

JACOB KEEPERMAN, MD

Assistant professor of anesthesiology and of emergency medicine

Keeperman serves as a member of the Midwest-1 Disaster Medical Assistance Team of the NDMS and works part time for Air Evac Lifeteam, a national helicopter emergency medical services company. As the Missouri medical director of an Air Evac operations team, he decides which aircrafts get sent to affected areas and what protocols will be followed. After Hurricane Harvey, Air Evac sent 16 aircraft from throughout the national fleet to Houston. There, team members delivered patients from flooded hospitals to dry medical centers, and patients in need of dialysis to dialysis centers outside of Houston. The company also sent aircraft to Florida in response to Hurricane Irma.



JOE FOWLER



COURTESY OF JIM FEHR

Jim Fehr, MD, far right, with physicians and nurses at Pavia Arecibo Hospital.

JIM FEHR, MD

Professor of anesthesiology and of pediatrics

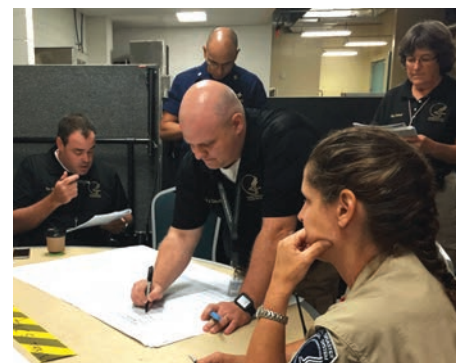
In hurricane-ravaged Puerto Rico, Fehr's main job as part of the federal government's Disaster Medical Assistance Team (DMAT) was to deal with nonemergency and logistical needs so health-care workers on the island commonwealth could concentrate on providing care to the sickest, most desperate residents. Fehr's team, including nurses from Barnes-Jewish Hospital and St. Louis-area physicians, pharmacists and paramedics, worked to prevent indirect deaths related to Hurricane Maria. Indirect deaths include, for example, a patient who dies because storm-damaged roads prevent her from refilling a life-saving prescription — or the loss of a patient who is dependent on a kidney dialysis machine in the midst of a power outage.

TY DAVISSON

Director of emergency management and business continuity

Davison, deployed to Puerto Rico with NDMS, helped coordinate the federal government's response to Hurricane Maria from an emergency command center in the San Juan Convention

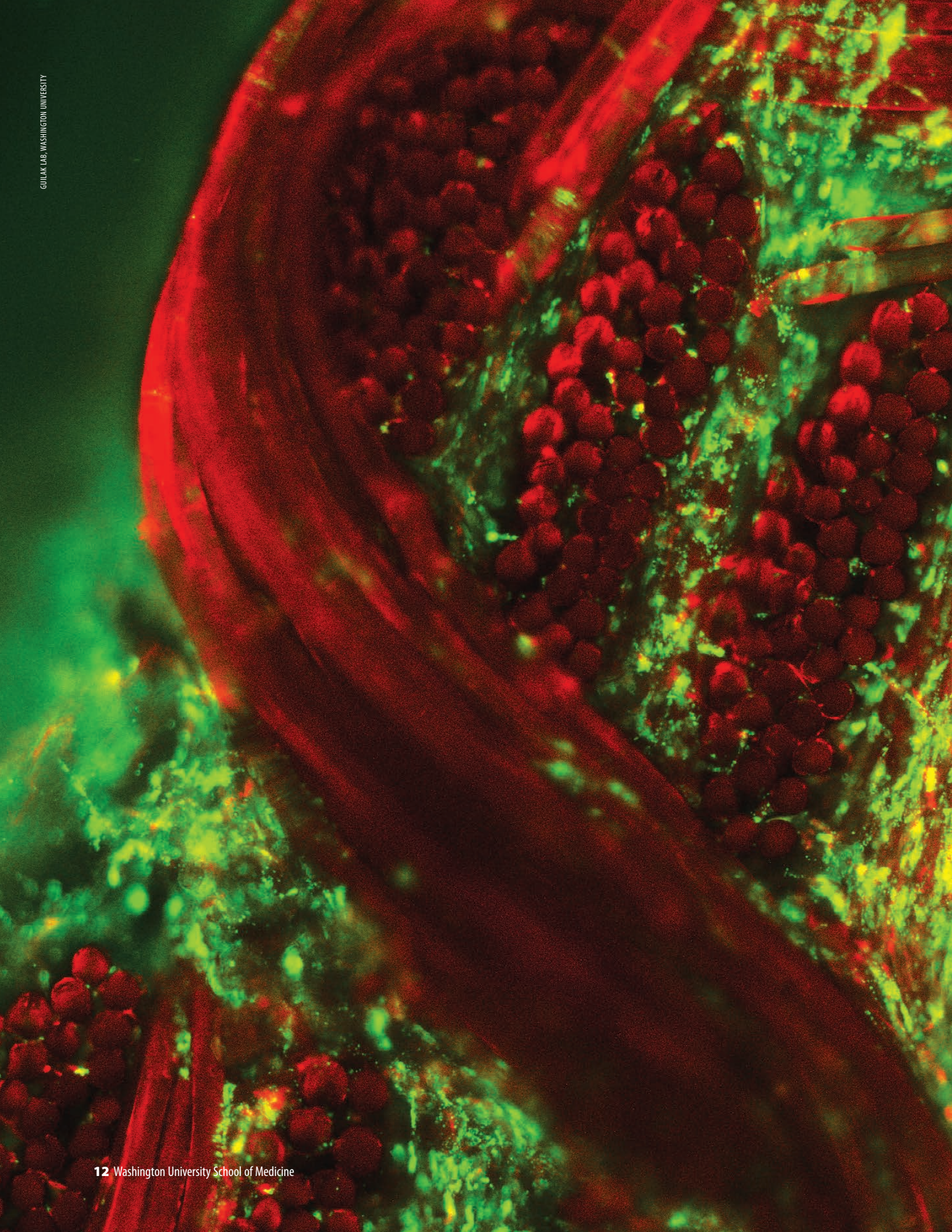
Center. For three weeks, he managed teams of medical staff (more than 1,000 people in all), mortuary workers, and public and behavioral health experts. To ensure an efficient medical response, each day the team planned, evaluated and tracked resources, determining where resources should go the following day.



COURTESY OF TY DAVISSON

Ty Davison, center, leads a meeting with federal response partners.

Air Evac Lifeteam sent a Missouri crew to Texas following Hurricane Harvey.





Lab-grown cartilage

Engineered stem cells could revolutionize arthritis therapy and joint replacement

BY JIM DRYDEN

Replacing a human joint is common, artificial and far from permanent. The procedure involves cutting into the body to remove living bone and replacing it with metal and plastic. As these parts typically last 15 to 20 years, a second — riskier — replacement surgery sometimes is necessary.

However, for a million Americans a year in agony with knee or hip arthritis, such implants are welcome. Because once cartilage, the tissue lining and lubricating joints, wears away, the patient is left with bone-on-bone pain, swelling, stiffness and disability.

School of Medicine researchers are working on a radically different way to help people with arthritis: creating living joint replacements from the patient's own cells and then programming those cells to fight an arthritis recurrence.

Farshid Guilak, PhD, and collaborators have successfully grown part of a living human hip joint in the lab and now are testing the methodology in animals. The development ultimately could transform how arthritis and some orthopedic conditions are treated. Moreover, aspects of the research have implications for a host of other diseases.

Stem cells, stained green, grow throughout the pores of a fabric scaffold, stained red, that is molded in the shape of a hip joint. After being treated with chemicals, the cells turn into cartilage. Eventually, the scaffold melts away, leaving a living replacement joint.

For Guilak, it all began with envisioning cells as machines.

“My background is in engineering, but I’ve always worked on cells,” said Guilak, a professor of orthopaedic surgery, of developmental biology and of biomedical engineering. “Cells are the basis of life, but they also are like little machines. They have motors. They store things like computers do, and they can generate forces and crawl around and pull on things.

“They’re little machines that happen to be alive, and we thought, ‘Why not treat them like machines and reprogram them to become what we want them to be?’ And our first thought was to make cells into things that can treat diseases automatically.”

Guilak, also the co-director of the Washington University Center of Regenerative Medicine and director of research for Shriners Hospitals for Children-St. Louis, is working in a field known as synthetic biology. Combining aspects of engineering and biology, researchers design and build new cellular components to do something different from what they do in nature.

Guilak manufactures cells programmed to combat arthritis. His lab is one of the few labs in the world doing this type of work. Until now, most synthetic biology research has been conducted in bacteria, which are easier to modify than cells.

“We began to work in mammalian cells, and it was difficult when we first started, but we got very lucky because as we were launching this research, the technique called CRISPR/Cas9 came on the scene, allowing us to quickly edit the genes in these cells,” Guilak said.

CRISPR/Cas9 technology enables researchers to alter DNA sequences and modify gene function.

Regrowing cartilage

Starting this process requires the manufacture of a basic building material: human cartilage. First, Guilak’s laboratory acquires stem cells from skin or subcutaneous body fat via liposuction. Then, the researchers treat those stem cells with substances that convert them into particular cell types. “If you pull those cells out of the body and give them a very defined set of proteins and genes, they’ll start to make cartilage or bone or even muscle,” Guilak said.

In this case, researchers treat the stem cells so that they grow into cartilage, one of the principal tissues damaged by arthritis.

But Guilak’s team was not content to use stem cells of ordinary “intelligence;” the researchers wanted to make them *smarter*. Using the gene-editing tool CRISPR/Cas9, the researchers excised a gene in

From left, Guilak, Shannon O’Connor, an MD/PhD candidate, and Lara Pferdehirt, a PhD student, examine samples from a recent stem cell study.



TIM PARKER

the cells associated with inducing inflammation and replaced it with a gene that dampens it. They dubbed these cells as “SMART” (Stem cells Modified for Autonomous Regenerative Therapy).

Inflammation is associated with all forms of arthritis and triggers much of its pain and discomfort. Osteoarthritis is a degenerative, inflammatory condition caused by wear and tear on specific joints. Rheumatoid arthritis, an autoimmune disorder, occurs when the immune system attacks tissues in joints as if they were foreign invaders.

Through an analysis of arthritic cartilage, Guilak’s former student Jonathan Brunger, PhD, found that a particular gene, activated by inflammation, sparks further inflammation in response to a molecule called tumor necrosis factor- α (TNF- α). This molecule is primarily responsible for the inflammatory response in rheumatoid arthritis. Several available drugs block the TNF pathway to treat arthritis.

“These drugs work in about half of all patients,” Guilak said, “but they’re given at high doses continuously, even though the disease waxes and wanes. What you really want is something that’s only given when there is a flare in the disease.”

Such medications reduce inflammation, but also carry side effects; they can suppress the immune system, affecting the body’s ability to fight infection.

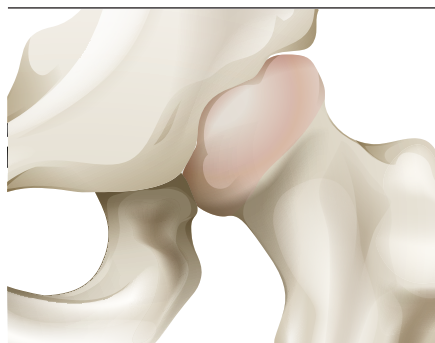
The gene that Guilak and Brunger inserted into the cartilage cells is activated only during bouts of arthritis inflammation, targeting the same pathway as the drugs Enbrel, Humira and Remicade. “We can control how a cell reacts to the external signals it receives,” Guilak said. “We can use CRISPR/Cas9 to make new logic circuits inside a cell.

“In this case, it’s called a closed feedback loop because the cell has the capacity to shut down something that’s happening in its environment. Instead of encountering an inflammation signal and amplifying it to get bigger and bigger, which is what happens in arthritis, now when these SMART cartilage cells see this inflammatory molecule, they make the drug inhibitor to block it.”

Arthritis and beyond

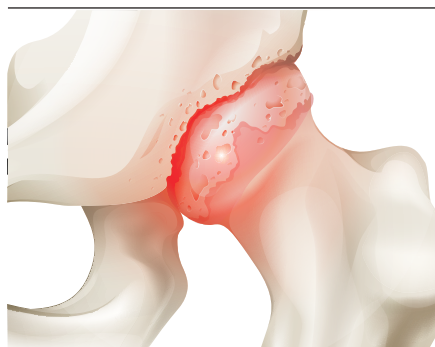
Guilak’s team is working to combat the differing types of arthritis. Solutions range from a living joint replacement made with SMART cells for localized osteoarthritis to a possible implant or vaccine for the systemic disorder rheumatoid arthritis. Encased SMART cells could be placed under the skin the same way Norplant birth-control

Treating degenerative joint disease



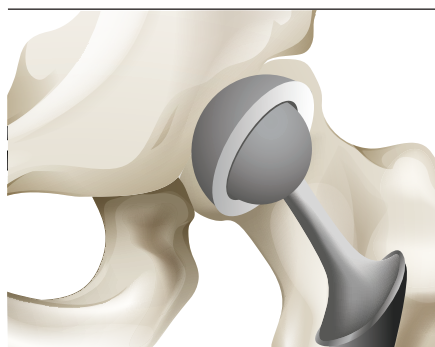
HEALTHY HIP JOINT

Healthy, smooth cartilage absorbs energy, bears weight and lubricates the joints for easy movement.



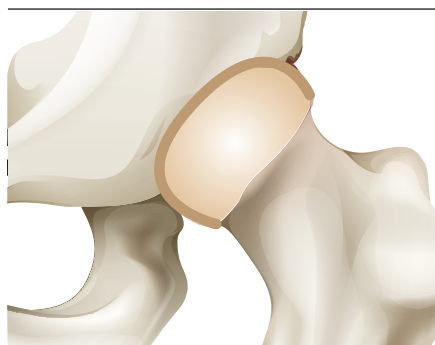
ARTHRITIC HIP JOINT

Degenerating cartilage results in bone-on-bone pain, swelling and stiffness.



ARTIFICIAL HIP JOINT

An artificial prosthesis eases pain and restores mobility but wears out in 15 to 20 years.

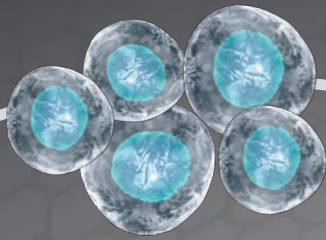


LIVING JOINT

Resurfacing the joint with newly grown human cartilage potentially could last longer with fewer side effects. Engineered cells could prevent an arthritis recurrence.

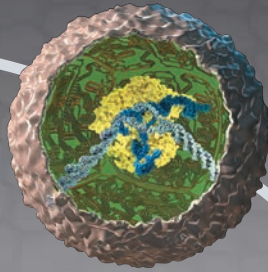
Rebuilding a human hip

One day, researchers may be able to resurface an arthritic joint using a patient's own stem cells.



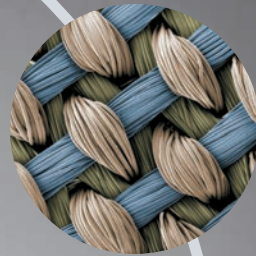
STEM CELLS

Stem cells are acquired from the skin or from subcutaneous body fat via liposuction.



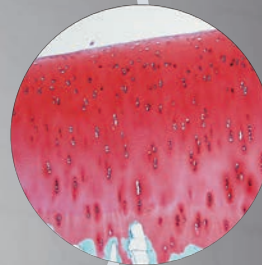
SMART CELLS

With gene-editing technology, the stem cells are rewired to fight arthritis.



SCAFFOLD

Cells are placed onto a porous, woven fabric molded into the shape of a hip ball. The cells permeate the fabric as it melts away.



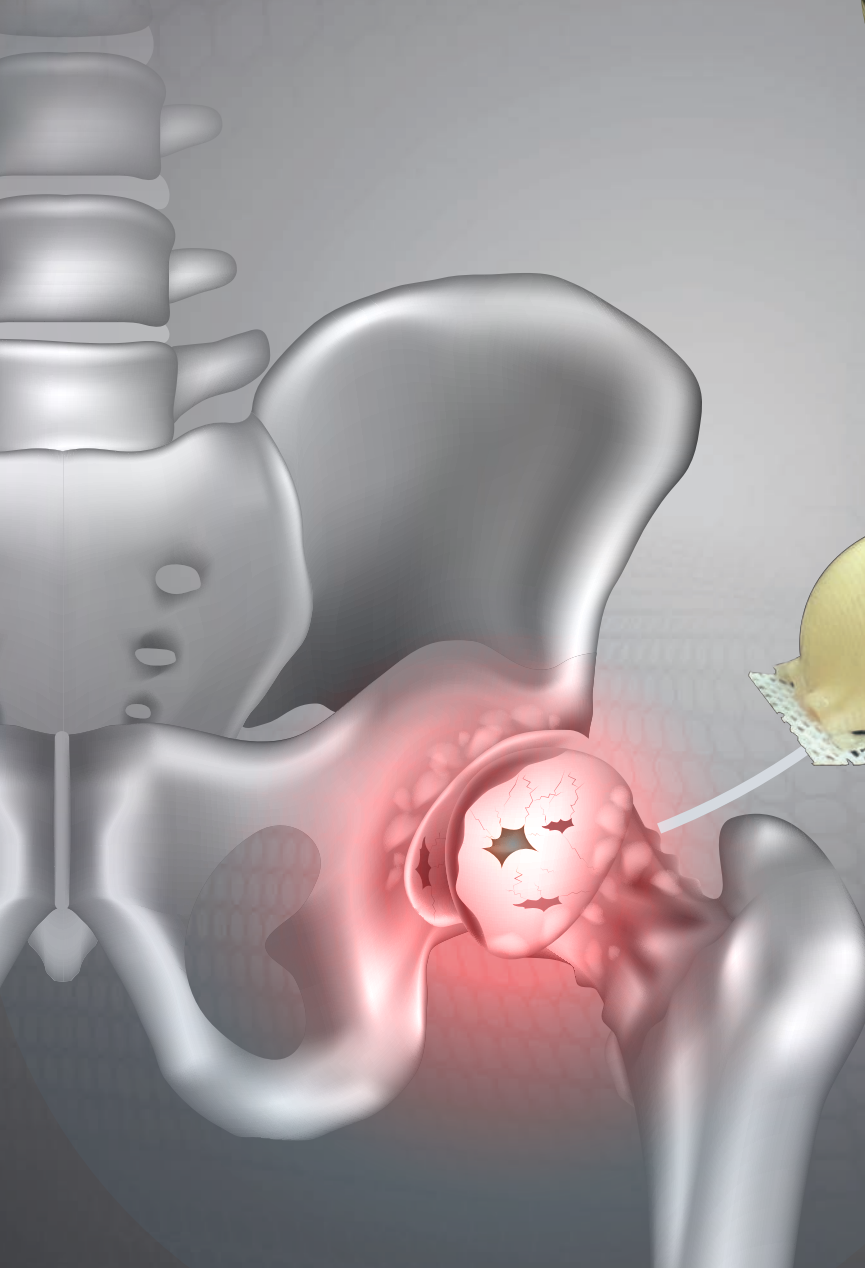
CARTILAGE

Following a chemical treatment, the cells change into cartilage.



SYNTHETIC HIP JOINT

Newly grown cartilage, with the ability to produce an anti-inflammatory drug, could keep the hip moving for years to come.



devices deliver hormones to prevent pregnancy for several months or years at a time. Likewise, because this strategy heightens immune response, a vaccine might be an effective biological treatment.

In all of these scenarios, it's possible, Guilak, said, that a patient could turn the gene on and off as needed by taking a pill. The idea is to protect the body both from inflammation and excessive medication.

One of Guilak's principal collaborators is Christine T. Pham, MD, a professor of medicine who treats patients with rheumatoid arthritis. Her lab has developed several mouse models of the disease, allowing researchers to test different treatment methods.

The researchers also have set their sights well beyond arthritis. Already, they are thinking about cellular feedback loops to deliver substances to fight other disorders, for example, cells that could be engineered to release insulin in response to high blood glucose.

For now, however, the primary strategy involves creating living cartilage from a person's own stem cells to ease pain and keep the disorder at bay.

A living prosthesis

Removing a worn-out artificial prosthetic can destroy the attached bone and put patients at risk for infection. Because of this, doctors are reluctant to perform artificial joint replacement in patients under age 50, leaving children and young adults with few options. Rising rates of obesity and arthritis mean that more people in their 40s are needing hip replacements.

SMART cartilage fashioned in the form of a living joint potentially could outlast those made of metal or plastic. Researchers also believe there's a lower risk of rejection because the cartilage cells are taken directly from the patient.

Stem cell treatments for osteoarthritis began as early as 2008. Mostly, doctors have injected stem cells directly into affected areas, hoping the cells would stay in place and turn into cartilage. But this method has proven unsuccessful, as the cells tend to float away within a couple of weeks.

Guilak has spent years working on a method to keep the new cartilage cells in the joint. Before coming to Washington University, he and his Duke University colleagues developed a way to weave 600 bio-compatible fibers approved by the U.S. Food and Drug Administration into a porous, high-performance fabric scaffold.



Using MRI images, the researchers can mold the fabric into the precise shape of a patient's joint and seed it with stem cells. "Over a six-week period, the cells go inside the fabric, start growing, and are given chemicals that turn them into cartilage cells. The fabric eventually melts away, leaving a hip made out of your own cells," Guilak said. "In the future, this technique could be used for any joints."

The weaving pattern makes the implant strong enough to withstand loads up to 10 times a patient's body weight — the standard force during exercise.

Guilak and the other researchers patented the weaving technique and formed a start-up company, Cytex Therapeutics Inc.

His laboratory has demonstrated the technique works in human cells in culture, and he's conducting animal studies that look very promising. As a result, Guilak has won the Arthritis Foundation's highest award, and the Proceedings of the National Academy of Sciences has published the findings. If those trials remain successful, human safety studies could begin in three to five years.

Despite worldwide media attention on the research, Guilak said he is most motivated by his daily walk to work. "Part of our lab is at Shriners Hospitals for Children," he said. "And we see so many kids come through with difficult problems. They have a whole lifetime ahead, but almost everything we do for them is temporary, or it's something like a metal-and-plastic implant, which isn't a great treatment for a child who will outlast those implants several times over.

"Seeing those kids is part of what drives us to find better solutions. Our concept is that we can make cells that are like tiny computers that sense what's causing problems and act accordingly.

"We're confident we're on the right track." □

Christine T. Pham, MD, one of Guilak's collaborators, is a professor of medicine who treats patients with rheumatoid arthritis. Her lab has developed mouse models of the disease, allowing researchers to test different treatment methods.



Leading *with* empathy

**The transformative influence of a doctor
who hasn't forgotten his past**

BY KRISTINA SAUERWEIN

Will Ross knows he should be dead. Before his teen years, he had been beaten and bloodied countless times and stabbed in the arm. He had witnessed an execution-style murder and had watched riots burn his community.

He had hidden in his house to avoid gangs. Indoors, he often buried himself in books to escape the alcohol-fueled fighting between his mother and her boyfriends.

"We were the poorest of the poor," Ross said. "However, my experiences with violence were not unique. Most of the kids I knew growing up are dead or in jail. It is not hyperbole to say I should be dead."

Now an esteemed nephrologist at the School of Medicine, Ross, MD, MPH, has achieved a level of success that he had never imagined as a boy scrounging for food and wearing ill-fitting hand-me-downs and fearing that rats would crawl over him in his sleep.



As part of an orientation program he designed, Will Ross, MD, MPH, exposes first-year medical students to blighted St. Louis neighborhoods — not unlike the ones of his own childhood.

Ross could easily ignore people living in communities like the ones of his childhood. But he won't. His early experiences inspire him as a physician, a professor of medicine and as associate dean of diversity. Long before buzzwords such as "health equity" emerged in the medical field, Ross was teaching how health outcomes are compromised by race, gender, sexual orientation, income, housing, education and other factors.

Through collaborations with local health agencies, Ross has initiated dozens of programs aimed at providing medical care to those who cannot afford it and at improving community resources necessary for good health, such as transportation to a health clinic or access to fresh fruits and vegetables.

"Humanity is lacking in neighborhoods like the one I grew up in," Ross said. "I understand the social and economic barriers and the anger rooted in the violence. As physicians, we must be aware of such obstacles to health care."

*"Humanity is lacking in neighborhoods like the one I grew up in
As physicians, we must be aware
of such obstacles to health care."*

Ross has ingrained these core principles of understanding and treating underserved patients into the medical school curriculum. He founded the Saturday Neighborhood Health Clinic for the sick and uninsured. More than 90 percent of Washington University medical students volunteer and gain practical, hands-on experience at the federally qualified, no-cost clinic. With faculty supervision, the students treat about 300 patients annually for ailments such as diabetes, asthma, high blood pressure and sexually transmitted diseases.

"Regardless of medical specialty interests, all students benefit from learning about public health, and not just from a clinical perspective," Ross said. "It teaches compassion and empathy. This is part of our moral responsibility as a medical school."

The same year Ross founded the Saturday Neighborhood Health Clinic — in 1996 — he also became the associate dean for diversity.

"Will Ross is empathetic, enthusiastic and brilliant, and as associate dean for diversity, he has been nothing short of phenomenal," said William Peck, MD, the Alan A. and Edith L. Wolff Distinguished Professor of Medicine and co-director of the Center for Health Economics and Policy.

Peck, who served for 14 years as executive vice chancellor and dean of the medical school, recruited Ross to the position.

"I knew right away that he was the person for the job," Peck said. "Dr. Ross seems laid back, but he isn't. He is strategic and determined in his trailblazing efforts. He has helped to transform public health care in St. Louis, the state, the country and the world, all while elevating Washington University in diversity and medical education."

Plunging into reality

Ross's influence on every student is visible beginning Day One. He created a mandatory, four-day orientation program for incoming medical students that includes a diversity retreat, lectures in health disparities and tours of St. Louis' poorest, most racially segregated nonwhite neighborhoods. Called Washington University Medical Plunge, the course removes students from academic and clinical settings and immerses them into the realities facing underprivileged patients.

On the tour, students see abandoned and dilapidated homes, weedy parks where feral dogs roam and a lack of basic services such as markets with healthy food.

"It defines the abstract," Ross said. "There's no sugar-coating. Some of the students have never witnessed poverty before the tour. It's important to broaden their outlook because they may one day treat patients in similar circumstances."

The tour leaves many students teary-eyed and emotionally altered. "It had a major impact on me professionally," said surgical resident Leisha Elmore, MD '13, MPH. "I found my love for serving underprivileged communities because of Dr. Ross."

Similarly, many Washington University students have said they chose the School of Medicine specifically because of Ross, who is known for keeping his office door open and spontaneously inviting them to his house, where he and nurse anesthetist Arlene Moore, his wife of nearly 30 years, raised two daughters. Both daughters are now adults dedicated to social justice.



WHITNEY CURTIS

Ross is noted for his calm demeanor and dapper clothing choices. He received his first bowtie for Easter when he was 4 years old. It's a fond memory that has contributed to a collection of 50 bowties.

At first glance, Ayodamola Otun, a first-year medical student from Nigeria, said he wondered if the distinguished professor with the bowtie would have time for him. "I thought Dr. Ross wouldn't be interested in me because he had lived in privilege long enough to forget about people like me. But I shared my personal challenges.

"It is hard to explain but the way he listened and responded showed me he cared. I felt safe and reassured that he was the right mentor, and Washington University was the right place," he said.

Ross's drive to improve medicine for the poor extends beyond his leadership in St. Louis. He has assisted in establishing health-care programs in Ethiopia and South Africa. Currently, in Haiti, Ross is helping to develop a university undergraduate program in public health. In the U.S., he has worked with the Centers for Disease Control and Prevention and other agencies to promote cultural awareness among physicians and reduce minority obstacles to health care. Through the Association of American Medical Colleges (AAMC), Ross advocates for increased diversity among faculty and students.

"Dr. Ross's work sits at the nexus of academic medicine and public health," said Juan Amador,

the AAMC's director of constituent engagement. "He is a national leader in this area."

A 2016 AAMC report attributed at least 40 percent of negative patient outcomes to health disparities caused by social and economic factors. Such inequities, the report stated, may cause "systematic, measurable and avoidable health differences between populations that stem from social factors such as racism, poverty, lack of healthful food, and homophobia that result in disproportionate disease and death for the poor, racial and ethnic minorities, persons living with disabilities, LGBT communities and others."

"Will Ross spoke about these issues when I first met him decades ago," said William Danforth, chancellor of Washington University from 1971 to 1995. "He was compassionate and authoritative, and I remember thinking, 'Gosh, that young man really knows what he's talking about.'"

Hiding from the violence

Ross knows because he lived it. Rarely has he spoken publically about his traumatic childhood. However, he has decided to share his experiences, hoping others will be inspired to persevere to achieve their goals.

Ross's journey began in a shotgun shack with four older siblings, his grandmother and

Ross often hosts dinner and impromptu gatherings for students at his Central West End home.



WHITNEY CURTIS

Standing before a memorial plaque, new medical students process the story of how 10-year-old Rodney McAllister was killed by a pack of stray dogs in a St. Louis park. The stop was part of a weeklong orientation focused on health disparities.

his mother in the small, segregated town of Helena, Ark. “I was born into a traumatic situation,” Ross recalled. “My mother’s boyfriend didn’t like me. My mother had mental health issues and was not there for me. I never knew my father. However, my grandmother, Willie Page, loved me unconditionally and, without doubt, was the biggest influence of my life.”

As a toddler, Ross’s family moved 90 miles north to Memphis to hide from his mother’s abusive boyfriend.

“My first memories were of violence,” Ross said. “I remember watching people hurt each other and not knowing what to say or how to process it.”

He aimed for inconspicuousness to avoid violent interactions. But he was lanky and wore big glasses, and his awkwardness and vulnerability grabbed attention. Ross fell prey to the older kids who assaulted him with rocks and bottles.

He devoured books from the library. He relished mathematical equations like other kids enjoyed sports. In kindergarten, he had his first memorable experience with medicine.

Ross’s sister, Helen, 6, had severe asthma exacerbated by their mother’s cigarettes. One night when the siblings were unsupervised, Helen could barely breathe. Ross and his other sister, Sherry, 8, helped walk Helen four blocks to an emergency room. Once they arrived, health-care workers groused, glared and ignored them.

“Will someone please take care of my sister?” the young Will Ross demanded. “She can’t breathe.”

“If you don’t like it,” a physician told the children, “leave.”

They didn’t, and eventually Helen was treated. But Ross never forgot the experience.

“I was 5 years old and as serious as I’ve ever been,” Ross said. “I told myself that if I ever became a doctor, I would never treat a patient so unkindly and disrespectfully as the staff had treated us. We were kids. We didn’t want Helen to die.”

Collectively, Ross’s neighborhood experienced its lowest point on April 4, 1968. For months prior, African-American sanitation workers had been on strike to protest economic and social injustices. Trash overflowed into the streets. An odor of human waste and rotten food prevailed. Flies buzzed in swarms.

“Still, we had glimmers of hope,” Ross said.

That’s because Martin Luther King Jr. had come to Memphis to support the sanitation workers. “He spoke of civil rights,” Ross said. “He was leading us toward a better life.”

However, shortly after 6 p.m., avowed racist James Earl Ray assassinated King at the Lorraine Motel, two blocks from Ross's neighborhood. "I remember my mother crying, neighbors crying," Ross said. "I was shattered. We all were."

For many, grief turned to anger. "Some people were armed and rioting," he said. "They began destroying non-black businesses. They burned down our neighborhood market run by Chinese-American immigrants. Their daughter, Shirley, was my friend. We did mathematical equations at the store. After the market was destroyed, I never saw her again. I have no idea what happened to the family."

Ross sighed heavily, gazed at the ground and shook his head in disappointment. "Another tragic outcome is that the neighborhood never recovered," he said. "To this day, it still looks bombed out."

A safe passage

Ross's future shifted one afternoon. With blood on his shirt — a result of a beating by gang members — he visited the high school guidance counselor.

The counselor pointed Ross toward Shirley and Alfred Wexner, who had established a scholarship fund in their deceased daughter's honor for underprivileged kids with academic promise.

Shirley Wexner helped Ross attend a summer program at Phillips Exeter Academy, an elite boarding school in New Hampshire. This exposed him to higher-level coursework and opportunities at elite colleges. Ross lived with the Wexners periodically in Memphis, usually during the harshest moments at his home.

"The Wexner family offered me a safe passage," Ross said. "In all likelihood, I would be dead if the Wexners hadn't intervened."

Like many students in the Exeter program, Ross was accepted into top-tier universities. He received a full-ride scholarship to Yale University, where he earned a degree in biology in 1980, and then to Washington University, where he earned a medical degree in 1984.

Throughout, the Wexner family provided financial and emotional support. "We love him," said Shirley Wexner's daughter, Barrie, who is slightly older than Ross. "We are proud he continues to help people in need."

Encounters with racism

Despite the Wexners' support, Ross had to overcome race-based obstacles. As a second-year medical student, Ross was interrogated, handcuffed and thrashed against a car hood. Police believed he had robbed a store for no reason other than his skin color. An hour later, Ross was released when a white classmate vouched that he had been in class when the robbery occurred.

The incident that most stands out occurred in 1985, when Ross was an internal medicine resident at a hospital affiliated with Vanderbilt University in Nashville.

"Around 2 a.m., a middle-age white man came into the emergency room with an inflamed knee," Ross recalled. "I told him I needed to drain the pus. He said he refused to be treated by a 'nigger doctor.' Those were his words. I took a deep breath and told myself to rise above and take the moral high ground."

"I said, 'Sir, my name is Dr. Ross. I'm your doctor. I'm not a nigger. I will be the person who treats you. But first, you owe me an apology.'"

The man apologized. In the years ahead, Ross would stand up to countless more racist acts.

"I feel there aren't that many 'bad' people; rather, there are those who have been socialized to think or act a certain way," Ross said. "Speaking out and showing them the damage done by their sometimes unintentional words or deeds can be insightful and even therapeutic, as they realize all of us have unconscious biases."

Ross continued: "As associate dean for diversity, I feel I should give voice to those who feel dispossessed but are either afraid to speak out or don't know how."

"By speaking out, we improve health care and we uplift humanity." □

In his nephrology practice, Ross makes a concerted effort to connect with patients and understand what's going on in their lives.



TIM PARKER





Esme "Ezzy" Hodge and her parents traveled from Bristol, U.K., for selective dorsal rhizotomy surgery with neurosurgeon T.S. Park, MD.

'Future we only dreamed of'

A renowned surgeon is restoring mobility in children with cerebral palsy

BY GAIA REMEROWSKI

As a baby, Alexa Reed seemed to be hitting all her developmental milestones. When it came time to walk, however, she started having trouble. Her right foot turned inward and she had a tendency to rise up on her tiptoes.

"For two years I asked her pediatrician if this was normal and if I should do something to fix it," said Amy, Alexa's mom. "We were told that she would grow out of it and that no intervention was needed aside from reminding her to walk flat-footed."

Over time, Alexa's muscles got tighter, she fell down frequently and increasingly relied on toe-walking. Wearing braces for several years and undergoing weekly physical therapy to stretch her tight legs did not improve the situation.

At nearly 4 years of age, Alexa finally received a definitive diagnosis: spastic diplegic cerebral palsy (CP), a chronic neuromuscular disorder that causes tightness and spasms in the extremities. Most commonly caused by lack of oxygen and early damage to the brain, spastic CP accounts for almost 80 percent of CP cases.

Soon after Alexa's diagnosis, the Reeds moved from Los Angeles to St. Louis for a new job and to be closer to family — not realizing that Washington University Medical Campus is home to T.S. Park, MD, a world-renowned, uniquely qualified pediatric neurosurgeon who specializes in treating spastic CP.

Post-surgery, Alexa, now 9, has full function and enjoys hiking, soccer and hanging out with friends. In Alexa and in thousands of other kids worldwide, Park has restored the ability to walk.

Not your average neurosurgeon

Park, the Shi H. Huang professor of neurosurgery, is a pioneer in the use of selective dorsal rhizotomy (SDR), a spinal surgery that he performs at St. Louis Children's Hospital. In the procedure, Park severs the nerves that cause spasticity.

Park has been performing SDR for 30 years, treating more than 3,700 patients from 47 states and 73 countries. Of those cases, only nine have ever required readmission (four for wound infections, five with spinal fluid leaks).

Amy found out about Park from an in-home physical therapist.

"It was glaringly clear that our move from Los Angeles back home to St. Louis was somewhat serendipitous," Amy said. "We were exactly where we needed to be to have the most skilled and successful surgeon on the planet be the one to end the grasp that spasticity had on our daughter for good, and give her a future we had only dreamed of."

Born in Bristol, U.K., Esme, or Ezzy (as she likes to be called) Hodge, had to come a bit farther for help. Ezzy's parents noticed their baby daughter wouldn't reach up for a cuddle and had trouble balancing independently. An MRI at age 2 revealed Ezzy had suffered a brain injury during birth. Like Alexa, she was diagnosed with spastic diplegic CP.

"We were told she would never walk," said Ezzy's mom, Angela. "As parents we were truly devastated."

Angela found Park's name during an online search for potential treatments. "I knew then I would do whatever it took to get Ezzy this amazing surgery and prayed Dr. Park would say yes to helping our little girl, as he was her only chance," Angela said.

In the initial patient evaluation, Park's team tells the family what type of outcome to expect: Will the child walk independently, or with crutches or a walker? Will the child be able to run and jump?

"I'm fairly sure we are the only ones who can give such a precise prediction," Park said. "Our prediction rate is very high — 85 percent correct."

Constantly seeking improvements

Severing spinal nerves that cause spasticity has been going on since the 1900s. But SDR did not make its way to the U.S. until 1986. Once Park learned about it in 1987, he began using the technique. By 1991, he made some key improvements.

The procedure originally involved cutting through five to six vertebrae in the lower spine to access the nerves causing spasticity. Park refined the process so he only needed to cut one lower vertebra. This less invasive method causes no long-term spinal problems and allows Park to perform the surgery on children as young as 2, who heal quickly, as well as patients as old as 50, whose spines would otherwise never heal completely.

Though Park performs the bulk of SDR surgeries on children, he also has operated on 130 adults — more than any other doctor in the world — at Barnes-Jewish Hospital.

Post-surgery, Alexa Reed, 9, of St. Louis, has regained full function.





Park celebrates with a gathering of former patients in the U.K. Patient families in other countries often throw welcome parties for Park whenever he visits to perform consults.

Neurosurgeons from across the globe come to observe his surgical methods and techniques. And Park trains fellows at Children's Hospital in the procedure.

Park also has published nearly 40 papers about the surgery in scientific journals. Because his team is the only one that has performed SDR surgery for three decades, it is in a unique position to study long-term outcomes.

Just this year, Park and his colleagues published two papers: In one, they followed 95 patients between the ages of 23 and 37 who had SDR surgery 20 to 28 years ago, and, in another, they surveyed 294 adult patients who had received SDR surgery as children. Both studies showed overwhelmingly positive results. The improvements these patients experienced in walking and in general quality of life after SDR surgery extended through adulthood and they reported no long-term side effects.

"We can clearly say SDR surgery is the only treatment that can remove spasticity permanently. No other treatment can do this," Park said.

"He developed — really single-handedly — the operation of selective dorsal rhizotomy for cerebral palsy," said Ralph Dacey, MD, the chair of neurologic surgery, in a 2017 tribute video honoring Park. "And not only did he develop the processes around doing that procedure very effectively and safely, but he was able to prove its efficacy in a series of papers that have become landmark studies."

Results "like magic"

The SDR surgery typically lasts three to four hours, followed by a five-day hospital stay. Then, the tough rehabilitation work begins. This includes daily physical therapy with Children's Hospital therapists. Out-of-country patients like Ezzy are expected to stay in St. Louis for about a month and then they must continue intensive physical therapy at home for a few more months while Park follows the progress remotely.

Ezzy's improvements began almost immediately after surgery.

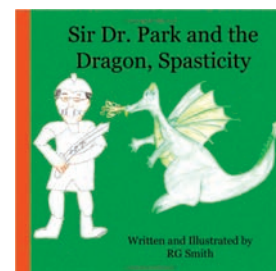
"Like magic before our eyes, she made daily improvements," Angela said this past October. "In just two short weeks, she has managed to walk with a cane, something I wouldn't have believed unless I saw it with my own eyes."

Some children, such as Alexa, need an additional orthopedic surgery to lengthen their muscles and/or tendons, which shorten from prolonged disuse.

Park refers these patients to pediatric orthopedic surgeon Matthew Dobbs, MD, who has developed a minimally invasive muscle- and tendon-lengthening surgery that further improves patients' range of motion and mobility.

The combined surgeries offer dramatic improvements in patients with severely impaired mobility, Park said.

Five months post-op, Alexa started playing sports like soccer and even participated in a 5K race.



Among the many patient tributes to Park: (top) a children's book titled "Sir Dr. Park and the Dragon, Spasticity" and (bottom) a doll made in his likeness.

Nine months after Alexa's surgery, Amy reported: "Dr. Park joyfully told my daughter, 'You never have to see my face again!' She was released from physical therapy and allowed to simply be a kid."

A global impact

To help spread the word about the life-changing surgery, in 2010, Park and his team started the Selective Dorsal Rhizotomy-St. Louis Children's Hospital Facebook page. It has since amassed 9,000 followers. Before long, family-run Facebook pages championing Park's expertise began cropping up — in Brazil, Korea and dozens of other countries.

Park checks the Children's Hospital and country-specific Facebook pages multiple times a day, replying to questions, posting comments,

medical literature and information to help parents and patients navigate the complex world of CP.

Park dedicates time every year to travel the world and examine children with CP to see whether they qualify for SDR surgery. To consult with these patients, he visits hospitals, clinics, sometimes even hotels, like the one owned by his brother in Korea.

Park also tirelessly advocates for health insurance policies to cover the surgery. He's given talks, for example, in Hungary to the country's national health insurance program director, and even testified to a British parliament member.

To help make the surgery financially accessible, especially for international families, Park lobbied Children's Hospital to set a fixed rate of \$40,000 for any patient paying out of pocket. Because of his undeniably positive outcomes, the hospital agreed. While many families must spend months



● Surgery patients from around the world

Park has performed selective dorsal rhizotomy on more than 3,700 patients from 47 states and 73 countries. In most cases, the procedure permanently removes spasticity, enabling the patient to walk again and resume age-appropriate activities. As a result, patient families continually send Park photos documenting the progress. Pictured above: former patients, their home country and year of surgery.

or years fundraising for the surgery, this fixed rate provides peace of mind. Park does his part by charging only \$100 for initial consults and nothing for follow-up visits.

Motivated by his international patient base, Park also worked to improve the hospital's interpreter service — something that benefits every non-English-speaking patient who comes through the doors.

Beyond grateful

"At the end of the day I know T.S. Park is what we call a guardian of childhood," said Joan Magruder, St. Louis Children's Hospital president, in a 2017 tribute video honoring Park. "He has done everything imaginable to make sure that every

child has the opportunity to be a child and to live their childhood to the absolute maximum."

This year, Missouri Gov. Eric Greitens and St. Louis Mayor Lyda Krewson declared Sept. 9 as Dr. T.S. Park Day. The day was marked by a symposium in Park's honor.

Families from every corner of the globe make videos showing their children's growth and progress and regularly post them on the SDR Facebook page — something Park said he loves to see. "I've befriended a number of parents," Park said. "We have personally become very connected."

It's a bond that Amy, and thousands of parents like her, acknowledge with gratitude. "The possibilities for Alexa are endless now," Amy said. "My daughter will live a full healthy life, free from spasticity, thanks to Dr. Park. He is our hero and will be family to us for life." □



Seth
USA
2009



Sara
Hungary
2011



★
Matthew
★ Australia
2013



Giovana
Brazil
2009



Personalizing medicine

**\$10 million gift drives
genome engineering
into therapeutic realm**

A **\$10 million gift** from longtime benefactors George and Debra Couch is supporting one of the School of Medicine's highest priorities: research advances in personalized medicine. In recognition of the couple's pledge, the university has named the newest research building on the medical school campus — a six-story facility located at 4515 McKinley Avenue — the Debra and George W. Couch III Biomedical Research Building. The couple was honored during an Oct. 6 dedication ceremony.

The gift establishes an endowed fund dedicated to initiatives aimed at revolutionizing the way disease is diagnosed, treated and prevented. Because personalized therapies often are rooted in a person's genetic makeup, the new fund provides support for the Genome Engineering Center (GEC). With the center's expertise in the latest genome-editing technologies, such as the ability to reprogram stem cells, university scientists are able to create precise cellular models of disease.

"We are deeply grateful to Debra and George Couch for their extraordinary generosity and for their commitment to improving human health," said Chancellor Mark S. Wrighton. "Their gift will support cutting-edge research by our talented faculty in pursuit of personalized medical solutions for patients. With this generous support, the Genome Engineering Center will be even better positioned as a resource for our investigators, who are working at the forefront of the biomedical sciences."

For the past 11 years, Couch has served on Washington University's Board of Trustees. He also has served as a member of the School of Medicine National Council for nearly two decades — giving him a close-up view of breakthroughs that have transformed the way scientists and physicians approach disease, from the sequencing of the human genome to research illuminating the key roles of the immune system and the gut microbiome in conditions such as cancer, obesity and malnutrition.

"It has been a privilege to be associated with the national council and be exposed to renowned faculty members who are making such a difference in the health of people around the world," he noted. "As my wife, Debra, and I began to think about our own legacy, we knew we wanted to help advance their work."

Powerful technology

Jeffrey D. Milbrandt, MD '78, PhD, the James S. McDonnell Professor of Genetics and head of the McDonnell Department of Genetics, established the Genome Engineering Center in 2013. This gift will help advance the center's innovative research and support services, particularly providing investigators with the ability to leverage a powerful DNA editing tool known as CRISPR-Cas9.

Developed only five years ago, CRISPR-Cas9 is revolutionizing biomedical research. "The technique allows us to edit genomes in a very precise way," Milbrandt said. "You use a computer to identify the exact DNA stretch you want to alter and then execute the change rapidly and efficiently. And you can use the same toolkit on any organism."

GEC experts employ CRISPR-Cas9 and other gene-editing techniques to create cells and cell lines with specific mutations and generate libraries of mutations



(Top) Chancellor Mark S. Wrighton delivered remarks at the dedication ceremony for the newly named Debra and George W. Couch III Biomedical Research Building. **(Middle)** A portrait of Debra and George Couch will hang in the building. **(Bottom from left)** Craig Schnuck, chair of the Washington University Board of Trustees; Wrighton; Debra Couch; George Couch; David Perlmutter, executive vice chancellor for medical affairs and dean of the School of Medicine; and Jeffrey Milbrandt, head of the McDonnell Department of Genetics, cut the ribbon.

that help investigators study disease processes, identify drug targets and advance new treatments.

The center also provides expertise in the manufacturing of induced pluripotent stem cells (iPSC). These are cells taken from skin, urine or blood and regressed back into stem cells. From there, they can be made into nearly any cell type. When taken from a person with a particular disease, these converted cells still model the disease process. This opens up new research opportunities, particularly in previously inaccessible cell types, such as neurons.

“The gift will serve as a catalyst for developing biological systems that model diseases in a highly personalized way and for facilitating the development of new diagnostics and therapeutics from biologically validated data — our best hope for discovering precise ways to alleviate human suffering,” said David H. Perlmutter, MD, executive vice chancellor for medical affairs and dean of the School of Medicine.

The GEC is a world leader in the production of engineered cells and cell lines. Since its inception, the center has created more than 300 CRISPR-modified cell lines, including more than 100 derived from iPSCs.

The center has provided services to 200 laboratories at Washington University and about 70 academic institutions and corporations around the globe. The center helps to catalyze the work of university researchers who do not have access to this groundbreaking technology in their own labs. With a thriving GEC as a resource, researchers can better compete for federal grant funding and departments can attract and retain top faculty.

According to Milbrandt, genome engineering and iPSC technologies are developing at breakneck speed. “To keep pace, we must constantly invest in research

and development,” he said. “This endowment will allow us to implement new techniques, invest in highly skilled personnel, and purchase equipment that will help us move genome editing into the therapeutic realm.”

In addition to the GEC and the Department of Genetics, the Couch Biomedical Research Building is home to numerous initiatives and centers, including the Edison Family Center for Genome Sciences and Systems Biology, the Center for Cellular Imaging, the Center for Multiple Myeloma Nanotherapy, the Optical Radiology Lab, and the Molecular Imaging Center, and includes research space for the Center of Regenerative Medicine and the departments of Medicine and Radiology.

Inspired to help others

For more than three decades, the Couch family has provided significant support to Washington University. George Couch attended high school in St. Louis before earning a bachelor's degree in economics from Stanford University and a master's degree in business administration from Harvard University. He is founder, chairman, president and chief executive officer of Couch Distributing Company in Watsonville, California, and his wife, Debra, owns the Debra C clothing boutique in Carmel, California.

The family's commitment to the school began in 1986 with a very personal motivation — the endowment of the Gregory B. Couch Professorship in Psychiatry in memory of George's brother, who developed schizophrenia in his teens before dying unexpectedly from a heart attack at age 31. A Washington University psychiatrist treated Gregory while the family was living in St. Louis.

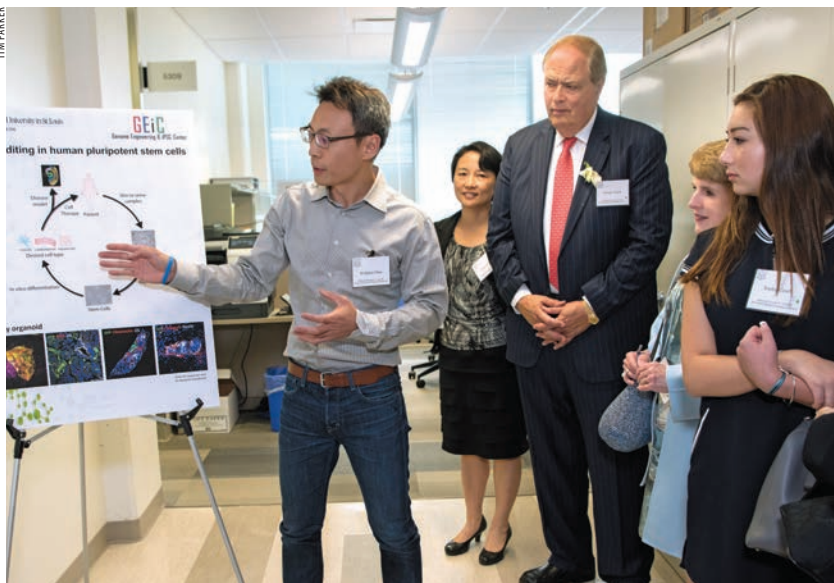
“Gregory was a wonderful person,” George Couch said. “His dream had been to attend medical school and become a doctor, so my family decided to endow a professorship in his memory at the School of Medicine.”

Deanna Barch, PhD, a renowned scientist who studies cognitive and language deficits in disorders such as schizophrenia, holds the professorship.

With the endowed fund in personalized medicine, the Couches saw a unique opportunity to help advance the quality of life for people around the globe by contributing to the next phase of discovery.

“If we are able to help mitigate suffering in any way, that's a larger contribution to humanity than Debra and I ever envisioned we would have,” George said. “We feel very fortunate that we can do something that has such potential to help others.”

Information for this story was provided by Mary Lee, Julia Evangelou Strait and Channing Suhl.



George Couch takes a tour of the research building.

Find your friends.

Classnotes are organized first by year of degree/training completion and then in alphabetical order.

How about you?

Share your news via the online form at wumcnews.org/classnotes. Submissions will be printed in a subsequent issue of Outlook magazine as space allows. Photos are welcome.

1950s



Wolff Kirsch, LA '51, MD '55, HS, serves as director of the Neurosurgery Center for Research, Training, and Education at Loma Linda University in California. Loma Linda

University Health honored Kirsch with the Distinguished Investigator Award in May 2017. His career accomplishments include: obtaining more than \$10 million in research grants and more than 40 U.S. and international patents, identifying two new amino acids in nature, publishing 200-plus papers and mentoring many graduate and medical students.

1960s

Paula Clayton, MD '60, recently moved to St. Louis City and is living within walking distance of the medical school, where she hopes to volunteer during the academic year.

Ira J. Kodner, LA '63, MD '67, was chosen by the St. Andrew's Charitable Foundation as a 2017 Ageless Remarkable Saint Louisan. These awards honor older adults



who remain an active force in the St. Louis metropolitan area and recognize the continued achievements of those who have made and continue to make a difference in lives.

Hunter Heath, MD '68, volunteers one day per week at Indiana University School of Medicine, and recently began volunteering as a workforce development consultant and adviser/editor on grant submissions for Fathers and Families Center, a nonprofit agency in Indianapolis, Ind. Fathers and Families seeks to reconnect a generation of young men with the tradition of responsible fatherhood through assistance in finishing high school or trade school, earning and keeping employment, and more. In his spare time, Heath enjoys learning how to play the guitar.

1970s

James M. Mick, MD '70, retired nearly four years ago, though he still enjoys serving as the medical director of the Partners for Healthy Students program at Yavapai Regional Medical Center in Prescott, Ariz. He recently traveled to Spain with his wife, Francine, and classmate Francisco "Paco" J. Garriga, MD '70, and reports that all had a great time. Mick enjoys spending time in church activities and with his family.

Timothy J. Ley, MD '78, HS, a leukemia researcher and hematologist at WUSM, has received a seven-year, \$6.4 million

Outstanding Investigator Award from the National Cancer Institute of the National Institutes of Health (NIH).

1980s

Jack Turman, PT '84, was excited to join the faculty at Indiana University's Richard M. Fairbanks School of Public Health as a professor in the Department of Social and Behavioral Sciences. Turman is dedicated to research, teaching and outreach to improve birth and infant development outcomes in local and global communities.

Bruce Alter, PT '86, was awarded Therapist of the Year at the annual Therapy in Educational Settings Conference in April 2017 from the Douglas Education Service District in Eugene, Ore.

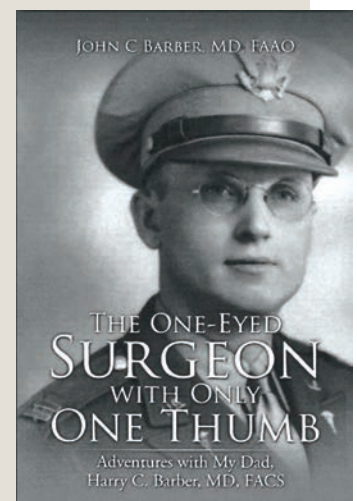
Christine Kushner, PT '87, of Homer Glen, Ill., proudly announced that her daughter was accepted into the Program in Physical Therapy at Washington University.

1990s

Angela L. Brown, MD '92, a hypertension management specialist within the WUSM Cardiovascular Division, was selected to receive the 2017 Hugh D. McCulloch Award from the Greater St. Louis Division of the American Heart Association.

Barber tributes father

John C. Barber, MD '65, of Pittsburgh, Pa., released a new book, "The One-Eyed Surgeon With Only One Thumb: Adventures With My Dad, Harry C. Barber, MD, FACS," in which he recounts how his father lost a thumb and one eye in a hunting accident at age 17, but persevered to graduate from the School of Medicine and have a successful career as a surgeon. Harry Barber also spent two years in the Arctic Circle during World War II repairing injured soldiers' injuries before returning home to Bloomington-Normal, Illinois. Harry Barber practiced during an era of \$5 office visits and \$8 house calls — although he was quick to reduce his fees and care for the indigent.





Audrey Shillington, MSW '87, PhD '87, GM '93, director of the School of Social Work at Colorado State University since 2012, also is assuming responsibilities as the associate dean

for academic affairs in the College of Health and Human Sciences. Additionally, she is professor of epidemiology at the Colorado School of Public Health. She has

published in the areas of psychometrics, epidemiology, prevention and intervention work aimed at adolescent and young adult risk behaviors. She has been principal investigator and co-investigator on National Institutes of Health, National Institute on Drug Abuse, National Institute on Alcohol Abuse and Alcoholism state grants totaling more than \$14 million. Her current work is focused on intervention and prevention efforts related to the changing landscape in legalized recreational marijuana use.



Kristin Will, OT '14, plays with children in a small Ugandan village.

Will helps establish Ugandan occupational therapy clinic

Occupational therapy alumna Kristin Will, OT '14, is transitioning from providing clinical care in the U.S. to working alongside the Musana Community Development Organization to start an occupational therapy clinic and outreach program in Iganga, a town in the eastern region of Uganda. Will plans to collaborate with Musana over a 15-month period to expand services in a health center and bridge social and medical projects.

Musana's mission is to provide the community with locally owned and operated sustainability projects, including schools, business loans, farming and social work. The organization has been working in the Ugandan community of Iganga for more than nine years.

From an early age, Will's parents exposed her to the need for international aid, and in high school she traveled to Kenya to assist with a medical education team. "I knew that I wanted to work internationally ever since," she said.

During her time at the School of Medicine, Will sought to use her training and skills to better understand the many internal and external factors that influence a person's life, from cognition and physical state to social capital and cultural influences. "I am excited to use the skills and knowledge that occupational therapy has given me to better understand the people in developing communities and to work together with them to bring sustainable development to their communities," Will said.

Frank Puc, PT '94, was named CEO at Revolution Physical Therapy Weight Loss based in the greater Chicago area.



Imran Zoberi, MD '96, HS '01, is a professor of radiation oncology at the School of Medicine, chief of the breast cancer service and chief of hyperthermia service in radiation oncology and serves as clinical director for radiation oncology at Barnes-Jewish West County Hospital.



Dawn Ebach, MD '98, was promoted to clinical professor at the University of Iowa Carver College of Medicine July 1, 2017. She is a pediatric gastroenterologist in the Stead Family Department of Pediatrics.

2000s

Julie K. Schwarz, MD '04, PhD '04, HS, has been named director of the Cancer Biology Division in the Department of Radiation Oncology at WUSM.

Joel C. Geerling, MD '08, PhD '08, is an assistant professor of neurology at the University of Iowa Hospital and Clinics.



Rahul Kasukurthi, MD '10, GM '10, looks forward to beginning his first post-fellowship attending job in plastic surgery at Kaiser Permanente in Portland, Ore.

2010s

Aaron Norris, MD '12, PhD '12, was selected to receive a Foundation for Anesthesia Education and Research (FAER) Mentored Research Training Grant. The grant is a two-year faculty award to "help anesthesiologists develop the skills, preliminary data for subsequent grant applications and research publications

needed to become independent investigators." Norris received the FAER grant for his project titled "Isoflurane Activated Neural Circuits," which will examine the functional relationship between neurons activated by isoflurane and neurons active during sleep.

Rogers pens science thrillers



Combining her passions for microbiology and literature, alumna Amy Rogers, MD/PhD '99, now writes and publishes science thrillers. A trainee

of the Medical Scientist Training Program, Rogers initially assumed she would work as a research scientist. As she began teaching undergraduate microbiology and molecular biology courses at California State University in the mid 2000s, Rogers found that she was "bursting with story ideas."

Acknowledging that she didn't know how to write fiction, Rogers began by writing critical reviews of any science thriller novels that she could find and launching a website, ScienceThrillers.com. Now, she is author of three published novels: "Petroplague," her debut book, "Reversion" and "The Han Agent."

"My goal with the science is to make it entirely plausible and accessible to the non-technical reader, while also keeping it as accurate as the story allows," Rogers said. All of her books feature interesting microbes, a female scientist as the protagonist, and at least one lab experiment that plays a critical plot role.

More information can be found at ScienceThrillers.com and AmyRogers.com.

Amit Patel, MD '12, HS '13, and Ami Patel, MD '12, HS '15, proudly announce the birth of their son, Avi Amit Patel, born on Aug. 4, 2017.



Lora Melman, LA '98, HS '13, is a fellowship-trained, board-certified and da Vinci robot-certified specialist surgeon in New Jersey who

is focused on providing cutting-edge surgical care by combining enhanced recovery methods with minimal-access techniques. She feels fortunate to have trained with prominent leaders in hernia, bariatrics and foregut surgery and her specific areas of interest include surgical weight loss for obesity, repair of all types of abdominal wall hernias, sport hernias, repair of diaphragmatic and hiatal hernias, treatment of esophageal dysmotility disorders, reflux disease and minimal-access adrenalectomy and splenectomy. Melman, an expert in the realm of hernia repair, is a widely published author of peer-reviewed literature on hernia repair biomaterials.

Yi Wang, MD '13, began working as a general pediatrician at Legacy Community Health in Houston.

Stephanie Weyrauch, GM '15, DPT '15, recently held a legislative day at her private practice, RehabAuthority Physical Therapy in Thief River Falls, Minn. The staff

welcomed Minnesota Congressman Collin Peterson while the team advocated for several issues, including physical therapy as an alternative to opioids for treatment of chronic pain, increased access to physical therapy services in rural areas, and repeal of the Medicare Therapy Cap. Local news reporters also attended and captured video on how physical therapy has helped some of Weyrauch's patients wean off opioids and live a more fulfilling life.



Jeffrey Fletcher Moley, MD, a highly regarded professor of surgery, chief of the Section of Endocrine and Oncologic Surgery and associate director at Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine, died Sunday, Oct. 15, 2017, at his home in Kirkwood following a sudden cardiac event. He was 64.



He had been married for 30 years to Kelle H. Moley, MD, the James P. Crane Professor of Obstetrics and Gynecology.

For more than two decades, Moley was a pioneer in researching and treating Multiple Endocrine Neoplasia (MEN), rare inherited syndromes that often cause an aggressive form of thyroid cancer and other endocrine diseases, particularly in those at young ages.

Moley was part of a team that identified the genetic mutations responsible for MEN syndromes and advanced a preventive procedure that includes surgical removal of the thyroid gland. Moley also operated on patients with recurrent thyroid cancer and other endocrine diseases.

"Jeff was a masterful surgeon," said Timothy J. Eberlein, MD, the Spencer T. and Ann W. Olin Distinguished Professor, head of the Department of Surgery, director of Siteman Cancer Center and surgeon-in-chief at Barnes-Jewish Hospital. "He delicately performed surgery to remove the thyroid gland in young children — some only a few months old — who were destined to develop an inherited form of thyroid cancer. The margin of error in these procedures is almost none, and Jeff was simply remarkable."

Besides treating patients at Barnes-Jewish and St. Louis Children's hospitals, Moley worked for more than three decades for the VA St. Louis Health Care System. At each of the hospitals, Moley helped train residents and medical students.

In addition to his wife, Moley is survived by: three sons, Patrick, Charles and John; his mother, Janis Walton Moley; a sister, Janis McCarthy; and a brother, Roger Moley.

Emerson Chairman Emeritus Charles F. Knight, a major benefactor of Washington University and longtime member of its Board of Trustees, died Tuesday, Sept. 12, 2017, of complications from Alzheimer's disease at Missouri Baptist Medical Center. He was 81.

Knight, who was chief executive officer at Emerson Electric Co. for 27 years, helped shape the present-day Washington University, according to Chancellor Mark S. Wrighton.

"Chuck Knight was a loyal and dedicated friend of Washington University for more than 40 years. His extraordinary generosity, support and vision can be felt and seen throughout our campuses," Wrighton said.

"He, along with his wife, Joanne, showed an unwavering commitment to advancing the university as well as the St. Louis community. Whether through helping establish Olin Business School as one of the premier institutions of business education and research in the world, or his critical support in building the Alvin J. Siteman Cancer Center into the country's third-largest cancer center, Chuck was dedicated to supporting institutions that improve lives and advance knowledge," he added.

A deep commitment to supporting medical research drove his support for the School of Medicine, where he had served on its National Council.

He and his wife established the Charles F. and Joanne Knight Distinguished Professorship in Orthopaedic Surgery, providing top-level teaching and research in this growing area.

The Joanne Knight Breast Health Center and Breast Cancer Program were dedicated in April 2007 in appreciation of the generosity and leadership of the Knights in supporting advancements in breast cancer research, patient care and community outreach at the Siteman Cancer Center at Barnes-Jewish Hospital and the School of Medicine.

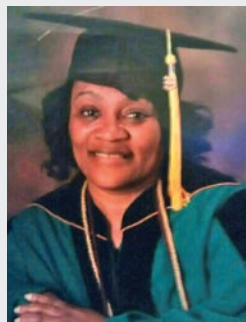
The Knights, longtime leaders in supporting Alzheimer's disease research, made a major commitment to the School of Medicine to advance Alzheimer's research. The university recognized the couple in 2010 by naming its world-renowned Alzheimer's Disease Research Center in their honor.

He served in a number of leadership capacities for Barnes Hospital, overseeing the creation of Barnes-Jewish Hospital and helping engineer the formation of BJC Health System, now known as BJC HealthCare.

He served as board chairman of the BJC system in the 1990s and was named emeritus chairman for life of Barnes-Jewish Hospital.

In 2002, Barnes-Jewish Hospital opened the Charles F. Knight Emergency and Trauma Center, a 52,000-square-foot facility offering 61 beds and a comprehensive environment for specialized care.

In addition to his wife, he is survived by children Lester Knight of Chicago, Anne Knight Davidson of St. Louis, Steven Knight of Seattle and Jennifer Knight Beckmann of Chicago; 12 grandchildren; and three great-grandchildren.



Denise Thomas, a medical assistant for 28 years in the Division of Hematology, died July 4, 2017, in St. Louis. Thomas, 52, died several days after suffering a stroke at her home.

Thomas was on track to earn a bachelor's degree in health-care management from University College in December. The college plans to award her degree posthumously.

Thomas is survived by her husband, Theo Thomas; her sons, Cory J., Phillip A. and Andrew A. Thomas; her sister, Vinissa Thomas; her brothers, Norval L.

Washington, Milton Bell,

Lamont Thomas and Frank P. Thomas; and six grandchildren.

For full obituaries, visit:
wumcnews.org/obits

1930s

Yvonne Bost Pickett, NU '38; Aug. '17

1940s

Ralph Berg Jr., MD '45; June '17

Juanita G. Brownback, NU '48; Aug. '17

J. Richard Compton, LA '40, MD '43; Aug. '17

Richard A. Jones, MD '43; Aug. '17

Jean J. Norwood, NU '43; Aug. '17

Irene M.C. Restad, OT '48; June '17

Harold Speert, HS '42; Feb. '17

William B. Stocker, DE '46; Aug. '17

1950s

Edwin E. Carter, MD '54; July '17

Rudolph E. Catanzaro, LA '49, MD '50; Aug. '17

Richard L. Ellis, DE '51; Aug. '17

William Y. Eubank, MD '53; July '17

Nancy Ferreira, OT '56; March '17

Ann Feldman Freeman, PT '59; Aug. '17

Guy T. Gillespie Jr., HS '54; June '17

Bill L. Hamilton, HA '56; Feb. '17

John W. Hard, LA '50, MD '54; Sept. '17

Bertram W. Justus, MD '57; May '17

M. Richard Katz, LA '52, MD '55; June '17

Leslie E. Long, DE '57; Sept. '17

Roy A. Nelson Jr., DE '57; Feb. '17

Havner H. Parish Jr., MD '56; June '17

Gonzalo T. Roman Jr., HS '59; Aug. '17

Paul A. Rubenstein, MD '57; July '17

Sidney L. Saltzstein, HS '58; May '17

Semon J. Sandven, MD '51; July '17

Jack C. Tippet, LA '49, MD '53; Aug. '17

Earl J. Wipfler Jr., LA '52, MD '55; Aug. '17

1960s

Martha Anne Coleman, GN '65; Apr. '17

Susan Hackman Kingston, NU '67; Sept. '17

Anne P. Lanier, MD '66; May '17

Robert T. Miller, MD '63; March '17

Paul M. Packman, LA '59, MD '63; Sept. '17

Symuel H. Smith, UC '61, HA '65; June '17

1970s

Richard Lewis Baron, MD '76; May '17

Jaswinder Kaur Ghuman, HS '79; Aug. '17

Pamela A. Pedersen, GR '71; Aug. '17

Robert Dale Rounds, DE '74; March '17

Thomas P. Wharton Jr., MD '71; April '17

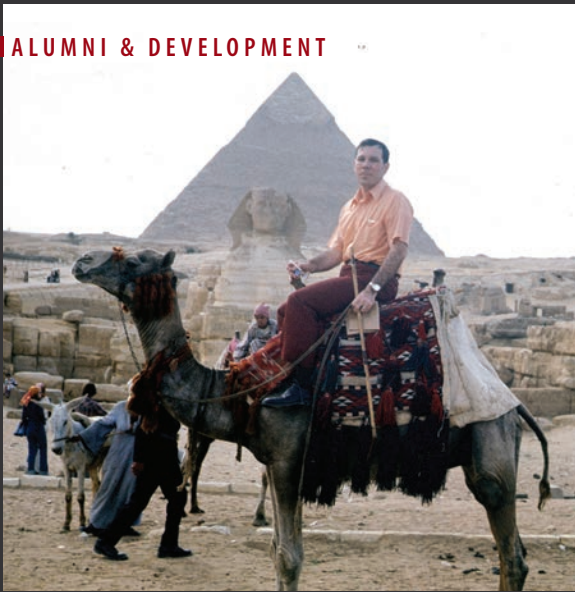
1980s

Jeanne Dahlen Lewis, MD '82; May '17

Richard Marias, DE '84; Aug. '17

1990s

Pamela Jo Smith, OT '92; June '17



James Wittmer in his many roles (clockwise from left): on a congressional trip to Cairo in 1975; with an aero club Cessna 150 in 1962; caring for a hurricane evacuee on a rescue helicopter in 1968; and in pressure suit training at a simulated altitude of 68,000 feet in 1962.

Flight surgeon's storied career

BY CHANNING SUHL

Standing in the cornfields near his Carlinville, Illinois home, a young James Wittmer, MD '57, MPH, watched in amazement as planes flew overhead.

A lifelong curiosity about the world around him — along with extraordinary leadership abilities — drove Wittmer to work on some of NASA's first human spaceflight programs, to lead Vietnam War triage operations, to travel the globe as an attending physician on congressional trips, and to direct health and safety in top U.S. corporations.

"Even as a child, I knew there was so much out there in the world, and I needed to see it and do it all," Wittmer said. "Washington University opened up the world to me — the one I'd only read about."

Wittmer, a retired colonel, attended undergraduate classes at Washington University and earned a medical degree from its School of Medicine. He and his wife, Juanita, an accomplished artist, are parents to three grown daughters and live in Texas. Recently, the couple committed estate gifts to fund professorships and scholarships on both campuses — supporting personalized medicine initiatives at the School of Medicine and the Driving Discovery project in Arts & Sciences.

As an undergraduate, Wittmer excelled in and out of the classroom, participating in intramural sports and Thurtene Honorary. During his medical school admission interview, he met C. Barber Mueller, MD, an educator and surgeon who had grown up on the same Carlinville street. Mueller became a valued mentor to Wittmer.

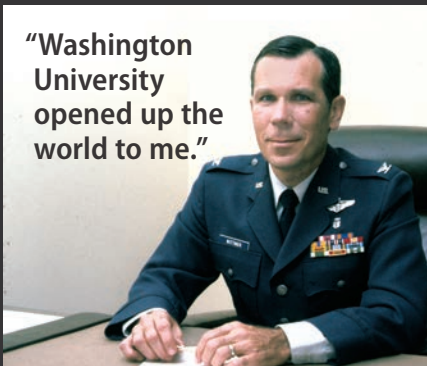
Following a surgical internship at the University of Virginia Hospital in 1958, Wittmer was drafted. He served two years as a U.S. Air Force flight surgeon and completed the USAF Aerospace Medicine Specialty Training Program. The first year of this training involved earning a master's degree in public health from Harvard University. He remembers being "swept up" in the country's space flight intrigue post-Sputnik.

Wittmer has the distinction of working on NASA's second human spaceflight program, Project Gemini, from 1965-67. In this pre-satellite era, NASA relied on crews deployed to ships around the world for real-time assessment of the astronauts.

Wittmer had minutes to check astronauts' vital signs and physiological responses as their spacecraft passed overhead and relay that data to Mission Control Center in Houston. He did this by monitoring a console that received information from electrodes attached to the astronauts' bodies.

After a 21-year Air Force career, Wittmer moved to New York, spending two years as U.S. medical director for Mobil Oil Corporation and 12 years with ITT Corporation, rising to corporate vice president for health, environment and safety.

"Washington University opened up the world to me."



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